Cerrahpaşa Med J 2023; 47(2): 229-234 ORIGINAL ARTICLE

# Evaluation of Coronavirus Disease 2019-Related Anxiety, Depression, and Post-Traumatic Stress Disorder in Liver Transplantation Recipients and Their Caregivers

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***Cite this article as:*** Adanır H, Erdoğan A. Evaluation of coronavirus disease 2019-related anxiety, depression, and post-traumatic stress disorder in liver transplantation recipients and their caregivers. *Cerrahpaşa Med J.* 2023;47(2):229-234.

***Abstract***

**Objective:** This study aimed to investigate the levels of anxiety, depression, and post-traumatic stress disorder in patients with liver transplantation and in their primary caregivers during the coronavirus disease 2019 pandemic.

**Methods:** Forty-five liver transplant recipients and 37 primary caregivers were included in the study. The sociodemographic data form, Hospital Anxiety and Depression Scale, Beck Anxiety Inventory, and the Post-Traumatic Stress Disorder Checklist—civilian version were administered to all participants.

**Results:** The mean age of the patients and caregivers was 51.46 ± 12.37 and 42.08 ± 15.04 years, respectively. Thirty-one percent of the patients and 70.3% of the caregivers were women. According to the Beck Anxiety Inventory, 13.3% of the patients and 21.6% of the caregivers had clinically significant anxiety, whereas 28.8% of the patients and 32.4% of the caregivers had clinically significant depression according to the Hospital Anxiety and Depression Scale scores. Post-traumatic stress disorder was determined according to Post-Traumatic Stress Disorder Checklist—civilian version in 33.3% of the patients and 48.6% of the caregivers. However, when the mean Beck Anxiety Inventory, Hospital Anxiety and Depression Scale, and Post-Traumatic Stress Disorder Checklist—civilian version scale scores of both groups were compared, no significant difference was found between the 2 groups. In the regression analysis, it was determined that each 1-point increase in Hospital Anxiety and Depression Scale depression scores resulted in a 1.314-fold significant increase in post-traumatic stress disorder scores.

**Conclusion:** The levels of depression and post-traumatic stress disorder are significantly higher in patients with liver transplantation and their caregivers during the coronavirus disease 2019 pandemic. Therefore, considering that these patients and their caregivers are not being treated for these disorders, the prompt identification of at-risk populations, early intervention, and effective management of diagnosed disorders are worthy of attention.

**Keywords:** COVID-19 pandemic, liver transplantation, depression, anxiety, post-traumatic stress disorder

## Introduction

A new coronavirus disease, named as coronavirus disease 2019 (COVID-19), was announced in Wuhan, a Chinese city, in December 2019. Slowly, it turned into an ongoing global epidemic, quickly and unpredictably, affecting millions of people.[1,2] One of the most affected groups during the COVID-19 period is solid-organ transplant recipients. High rates of hospitalization and intensive care unit admissions are reported among solid-organ transplant recipients infected with COVID-19, with mortality rates as far as 20%.[3] Solid-organ recipients have been one of the groups most affected by the pandemic process due to reasons such as high mortality. Solid-organ recipients, who are affected financially and socially, have been adversely affected, especially psychologically, during the pandemic process.[4] Indeed, the COVID-19 pandemic has been associated with perceived stress, sleep disorders, anxiety, depression, and post-traumatic stress disorder in solid-organ recipients.[5,6] It is known that depression is very common in organ transplant recipients. Rates of post-transplant depression in organ transplant recipients range from 5% to 75% for kidney transplant recipients and 13.7% to 67% for liver transplant recipients. Depression has been associated with worse outcomes in organ transplant recipients. Pre- and post-transplant depression has been associated with increased mortality, graft loss, post-transplant cardiovascular complications, increased healthcare utilization, poor compliance, and worse overall quality of life.[7] Anxiety rates are also known to be high in transplant recipients during the first few years after transplant.[8]

Based on experience from previous outbreaks, patients with chronic health conditions are most susceptible to the stress of crises such as pandemics. This vulnerability can also increase mental problems. Organ transplant recipients are also such a vulnerable group.[9] In kidney transplant recipients, the presence of a previous rejection episode and a history of COVID-19 infection in themselves or their close relatives were associated with anxiety level, while perceived high stress was reported as an independent predictor of anxiety and depression.[5] In liver transplant recipients, factors such as the presence of biliary complications and hepatocellular carcinoma, low income, and monthly admission to the hospital were associated with depression and anxiety.[10]

Coronavirus disease 2019 can cause mental problems in caregivers as well as in patients. Increased anxiety and mood disorders

**Received:** November 28, 2022 **Accepted:** January 13, 2023
**Publication Date:** August 22, 2023
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**DOI:** 10.5152/cjm.2023.22116

were reported in caregivers of solid-organ transplant recipients during the pandemic period.[11] In a study of caregivers of pediatric liver recipients, the majority of caregivers endorsed feeling anxious about the COVID-19 pandemic, with most reporting high stress especially about their child being immunosuppressed.[12] However, no study has been found in the literature search on the effect of the pandemic on the mental health of the caregivers of adult liver transplantation recipients.

Therefore, in this study, it was aimed to investigate anxiety, depression, and post-traumatic stress disorder in liver transplant patients and their primary caregivers during one of the most intense periods of the COVID-19 pandemic. Our H1 hypothesis is that liver transplant recipients and their caregivers have high levels of depression, anxiety, and post-traumatic stress disorder during the pandemic. Another hypothesis is that psychopathologies are more common in organ transplant recipients than in their caregivers, and there is a significant correlation between depression, anxiety, and post-traumatic stress disorders in these susceptible groups. Our study will reveal psychopathologies in a very vulnerable group, such as liver transplant recipients and caregivers, in times of crisis such as pandemics. It will make important contributions to the current literature by enabling us to better recognize the psychopathologies of this special group.

## Methods

### Participants

It is a cross-sectional study and was conducted between August 2020 and December 2020 at Akdeniz University Hospital Transplantation Center. Forty-five patients with liver transplantation and 37 primary caregivers were included in the study. Inclusion criteria in the patient group were determined as being over the age of 18, being at least primary school graduate, having passed at least 3 months after liver transplantation, and not being hospitalized with any active complications. Inclusion criteria in the caregiver group were determined as being over the age of 18, at least primary school graduate, and having been providing regular care to the same patient for at least 1 year. Patients with active substance or alcohol use, mental retardation, complicated comorbid disease (e.g., uncontrolled or complicated diabetes mellitus, hypertension, metastatic or advanced malignancy, active infection, and moderate-to-advanced chronic obstructive pulmonary disease) were excluded. Individuals with a previous history of psychiatric illness and currently receiving psychiatric treatment were excluded from the study. Also, those who had COVID-19 before were excluded from the study.

### Measures and Instruments

A sociodemographic data form including age, sex, education, work status, marital status, family income, and the number of persons they live with (if there was any) was filled out for each patient and caregiver at interviews. The nature of the liver donor (cadaver or living donor) for patients and for the caregivers the presence of chronic disease (if any), the nature of the care provided, and whether they received help for care were also noted, The Hospital Anxiety and Depression Scale (HADS),[13] The Beck Anxiety Inventory (BAI),[14] and The Post-Traumatic Stress Disorder Checklist—civilian version (PCL-C)[15] were administered to all participants. During the interview, whether close and distant relatives had COVID-19 infection and the difficulties experienced due to the pandemic (not being able to go out, difficulty in presenting to health institutions, social isolation, financial problems, family problems, and difficulty in accessing the home of the patient he cared for due to complete closure) were also questioned and recorded.

**The Hospital Anxiety and Depression Scale:** It is a 4-point Likert-type scale developed to measure depression and anxiety levels in patients with a chronic disease and in healthy individuals. It contains 14 questions in total. Seven questions measure anxiety and 7 questions measure depression. The cutoff point for depression was 7 points, and the cutoff point for anxiety was 10 points.

**The Beck Anxiety Inventory:** The scale consists of 21 items and is in 4-point Likert type. Thirteen items assess subjective anxiety and 8 items assess somatic symptoms. A maximum of 63 points can be obtained from the scale. The cutoff point was reported as 17 points.

**The Post-Traumatic Stress Disorder Checklist—Civilian Version:** It is a self-report scale that is used to evaluate symptoms related to nonmilitary traumas. The instrument comprises 17 items based on the diagnostic criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) for post-traumatic stress disorder. Thus, the first 5 items refer to the reexperience symptom group (criterion B), the next 7 items refer to the emotional avoidance/numbing (criterion C), and the last 5 items address hyperarousal (criterion D). In the filling-in instructions of the PCL-C, the patient is asked to report how much he/she has been bothered by the listed problems and complaints in the past month (not at all, a little bit, moderately, quite a bit, or extremely). The PCL-C may be preferred over other self-report measures because (a) its items evaluate the symptoms that are part of the DSM-IV diagnostic criteria, (b) its items may concern specific traumatic events, and (c) it addresses both the occurrence and the severity of symptoms. The cutoff score was determined as 22 points.

All stages of this study were carried out in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants who voluntarily participated in the study. Written ethics committee approval was obtained from Akdeniz University Faculty of Medicine Clinical Research Ethics Committee for our study (Date: September 9, 2020, Number: KAEK-705).

### Statistical Analysis

Statistical Package for Social Sciences 23.0 (IBM SPSS Corp.; Armonk, NY, USA) program was used for analysis. The Kolmogrov–Smirnov test was used for the assumption of normality. Descriptive variables are given as mean ± SD, percentage, and number. The chi-square test was used in the analysis of categorical data. In the comparison of the 2 groups, the *t*-test was used when the data were in a normal distribution, and the Mann–Whitney *U*-test was used in cases where the data did not fit the normal distribution. Binary logistic regression was used to examine whether depression, anxiety, and sex were associated with the likelihood of having post-traumatic stress disorder (PTSD). A *P*-value <.05 was considered statistically significant.

## Results

In our study, the mean age of the patients was 51.46 ± 12.37 years, and the mean age of the caregivers was 42.08 ± 15.04 years ($P = .003$). About 31.1% of the patients (n = 14) and 70.3% of the caregivers (n = 26) were women ($P < .001$); other sociodemographic data are summarized in Table 1.

The presence of past COVID-19 infection in close and/or distant relatives (if any) and the difficulties experienced due to the pandemic are presented in Table 2.

The mean HADS depression subscale scores were 4.60 ± 3.94 in patients and 4.83 ± 3.88 in caregivers ($P = .779$). The mean

**Table 1.** Sociodemographic Data of the Participants

| | | Patients (n = 45) | | Caregivers (n = 37) | | |
|---|---|---|---|---|---|---|
| | | n | % | n | % | *P* |
| Sex | Female | 14 | 31.1 | 26 | 70.3 | ***<.001*** |
| | Male | 31 | 68.9 | 11 | 29.7 | |
| Education | Elementary school | 21 | 48.8 | 12 | 32.4 | .262 |
| | High school | 11 | 25.6 | 15 | 40.5 | |
| | University | 11 | 25.6 | 10 | 27.0 | |
| Employment status | Working | 9 | 20.9 | 5 | 13.5 | .384 |
| | Not working | 34 | 79.1 | 32 | 86.5 | |
| Marital status | Married | 32 | 76.2 | 20 | 54.1 | .062 |
| | Not married | 9 | 21.4 | 12 | 32.4 | |
| | Divorced | 1 | 2.4 | 5 | 13.5 | |
| Lives with | Family | 42 | 95.5 | 33 | 89.2 | .286 |
| | Alone | 2 | 5.5 | 4 | 10.8 | |
| Income (Turkish liras) | 0-2499 | 18 | 41.9 | 14 | 38.9 | .898 |
| | 2500-7500 | 15 | 34.9 | 12 | 33.3 | |
| | 7500 and more | 10 | 23.3 | 10 | 27.8 | |
| Donor | Cadaveric donor | 9 | 20.9 | | | |
| | Living donor | 34 | 79.1 | | | |
| Chronic disease in caregiver | Yes | | | 15 | 40.5 | |
| | No | | | 22 | 59.5 | |
| Nature of care | Living with the patient | | | 31 | 83.8 | |
| | Lives in her/his own house | | | 5 | 13.5 | |
| | Rare visits | | | 1 | 2.7 | |
| Someone who helps the caregiver | Yes | | | 9 | 24.3 | |
| | No | | | 28 | 75.7 | |
| Age (years), mean ± SD | | 51.46 ± 12.37 | | 42.08 ± 15.04 | | ***.003*** |

Bold and italic values in $P < .05$.

**Table 2.** The Difficulties Experienced Due to the COVID-19 Pandemic

| | | Patients (n = 45) | | Caregivers (n = 37) | | |
|---|---|---|---|---|---|---|
| | | n | % | n | % | *P* |
| Close relative with COVID-19 infection | Yes | 8 | 21.1 | 9 | 25.0 | .687 |
| | No | 30 | 78.9 | 27 | 75.0 | |
| Distant relative with COVID-19 infection | Yes | 18 | 43.9 | 10 | 27.8 | .142 |
| | No | 23 | 56.1 | 26 | 72.2 | |
| Inability to go out | Yes | 29 | 65.9 | 22 | 59.5 | .549 |
| | No | 15 | 34.1 | 15 | 40.5 | |
| Difficulty in presenting to the hospital | Yes | 6 | 13.6 | 8 | 21.6 | .344 |
| | No | 38 | 86.4 | 29 | 78.4 | |
| Social isolation | Yes | 28 | 63.6 | 25 | 67.6 | .711 |
| | No | 16 | 36.4 | 12 | 32.4 | |
| Financial problems | Yes | 15 | 34.1 | 16 | 43.2 | .399 |
| | No | 29 | 65.9 | 21 | 56.8 | |
| Family problems | Yes | 4 | 9.1 | 6 | 16.2 | .335 |
| | No | 40 | 90.9 | 31 | 83.8 | |
| Inability to reach the patient he/she cares for | Yes | | | 5 | 13.5 | |
| | No | | | 32 | 86.5 | |

COVID-19, coronavirus disease 2019.

HADS anxiety subscale scores were 4.51 ± 3.73 in patients and 4.27 ± 3.44 in caregivers ($P = .829$). The mean BAI scores were 7.40 ± 8.82 in patients and 9.32 ± 9.34 in caregivers ($P = .319$). The PCL-C mean scores were 18.60 ± 12.04 in patients and 18.94 ± 14.50 in caregivers ($P = .906$). The comparison of the scale scores of the groups is presented in Table 3.

The rates of participants scored above the cutoff points of the scales were also evaluated. According to the BAI scale, 13.3% of the patients and 21.6% of the caregivers were diagnosed with anxiety disorder. Similarly, according to the HADS depression subscale, clinically significant depression was found in 28.8% of patients and 32.4% of caregivers, and according to the HADS anxiety subscale, clinically significant anxiety was observed in 8.8% of patients and 5.4% of caregivers. The PCL-C scores were also above the cutoff point in 33.3% of patients and 48.6% of caregivers, indicating PTSD at the clinical level.

In addition, the correlations between the scales applied to all participants were evaluated, and the findings are summarized in Table 4.

A preliminary analysis suggested that the assumption of multicollinearity was met (tolerance = .33). The model was statistically significant, $\chi^2$ (4, n = 82) = 40.666, $P < .001$, suggesting that it could distinguish between those with and without PTSD diagnoses. The model explained between 39.1% (Cox & Snell $R^2$) and 52.8% (Nagelkerke $R^2$) of the variance in the dependent variable and correctly classified 80.5% of cases. Participants were found to be 1.314 times more likely to have PTSD for each 1-point increase in the depression score. Other variables did not predict PTSD Table 5.

## Discussion

In our study, the mean BAI, HADS, and PCL-C scale scores of both groups were found to be similar, indicating that they have been experiencing similar difficulties during the pandemic. When the scale scores are evaluated for each participant individually, 13.3% of the patients and 21.6% of the caregivers had clinically significant anxiety, whereas 28.8% of the patients and 32.4% of the caregivers had clinically significant depression. Post-traumatic stress disorder was determined in 33.3% of the patients and 48.6% of the caregivers. In addition, a positive correlation was found

**Table 3.** Comparison of the Scale Scores of the Groups

| | Patients, mean ± SD (n = 45) | Caregivers, mean ± SD (n = 37) | *P* |
|---|---|---|---|
| Beck Anxiety Inventory | 7.40 ± 8.82 | 9.32 ± 9.34 | .319 |
| Hospital Anxiety and Depression Scale—Depression | 4.60 ± 3.94 | 4.83 ± 3.88 | .779 |
| Hospital Anxiety and Depression Scale—Anxiety | 4.51 ± 3.73 | 4.27 ± 3.44 | .829 |
| The Post-Traumatic Stress Disorder Checklist—civilian version | 18.60 ± 12.04 | 18.94 ± 14.50 | .906 |

**Table 4.** Correlations Between Scales Applied to All Participants

| | Age | BAI | HADS Depression | HADS Anxiety | PCL-C |
|---|---|---|---|---|---|
| Age | | 0.025 | 0.019 | –0.044 | –0.134 |
| BAI | 0.025 | | ***0.615**** | ***0.780**** | ***0.670**** |
| HADS depression | 0.019 | ***0.615**** | | ***0.678**** | ***0.578**** |
| HADS anxiety | –0.044 | 0.780 | 0.678 | | 0.617 |
| PCL-C | –0.134 | ***0.670**** | ***0.578**** | ***0.617**** | |

Bold and italic values in $P < 0.05$. n = 82. All values are correlation coefficients.
BAI, Beck Anxiety Inventory; HADS, Hospital Anxiety and Depression Scale; PCL-C, The Post-Traumatic Stress Disorder Checklist—civilian version.

between BAI, HADS, and PCL-C scores. Accordingly, the higher the BAI score, the higher the HADS depression and anxiety scores. Similarly, as HADS depression scores increased, HADS anxiety and PCL-C scores also increased.

In the present study, anxiety levels were 13.3% and 21.6% for patients and caregivers, respectively. For the general population, the prevalence of any anxiety disorder among adults is estimated to be 19.1%.[16] Looking at more specific groups, in a study conducted during the COVID-19 pandemic in kidney transplant patients, it was reported that 23.6% of patients had anxiety, with higher levels of anxiety in patients with a history of COVID-19 infection in their own or close relatives, and in patients with a history of rejection at any time.[5] In a cross-sectional study conducted with 305 organ transplant recipients in Wuhan at the beginning of the pandemic, the anxiety rate was reported to be 6.9%.[6] In studies evaluating caregivers of liver transplant recipients, higher levels of anxiety have been reported in relation to COVID-19.[11,12] In our study, patients and caregivers had similar and slightly lower levels of anxiety with the general population. During the COVID-19 pandemic period, there have been strict pandemic restrictions in our country. Due to these restrictions, the transmission concerns of individuals may have decreased, and therefore, their anxiety levels may have been found to be similar to pre-pandemic levels despite the COVID-19 pandemic.

Depression is also a common mental disorder. The prevalence of depression in adults worldwide is estimated to be 5%.[17] Depression levels reported during the pandemic are higher than the pre-pandemic period. Indeed, in a study conducted in the last quarter of 2020, depression was reported in 44.3% of kidney transplant recipients.[5] In another study conducted with 63 patients (49 lung transplantation recipients and 14 transplantation candidates), depression was found in 17.46% of patients in relation to the pandemic.[18] In another study conducted with 48 pediatric solid-organ recipients, 96 caregivers, and 48 healthy controls, an increase in mood disorders (71.9%) and deterioration in sleep quality (64.6%) were reported in caregivers.[8] Looking at liver transplant recipients, they have been found to display significant risk aversion behavior and have a high perception of loneliness during the pandemic.[19] Similarly, in our study, a high rate of depression was found in both patients and their caregivers. During the pandemic in our country, strict restrictions were applied—individuals had to spend time alone at home and stayed away from social activities. An information overload had been created by the media about the fact that immunosuppressed patients were at higher risk. This perception of risk may have prompted more social isolation and increased the rates of depression. These results emphasize the importance of providing social and psychological support, especially in liver transplant recipients and caregivers.

Trauma can be defined as an emotional response to a terrible event including but not limited to any kind of accidents, violence,

**Table 5.** Logistic Regression Analysis to Determine the Predictors of Post-traumatic Stress Disorder

| | | | | | | | 95% CI OR | |
|---|---|---|---|---|---|---|---|---|
| | *B* | SE | Wald | *df* | *P* | OR | LL | UL |
| Constant | –8.208 | 2.934 | 7.823 | 1 | .05 | 0.000 | | |
| Beck Anxiety | 0.125 | 0.070 | 3.233 | 1 | .072 | 1.133 | 0.989 | 1.299 |
| HAD depression | 0.309 | 0.120 | 6.621 | 1 | ***.010*** | 1.362 | 1.076 | 1.724 |
| HAD Anxiety | –0.055 | 0.163 | 0.115 | 1 | .735 | 0.946 | 0.687 | 1.303 |
| Sex | 0.687 | 0.755 | 0.829 | 1 | .363 | 1.988 | 0.453 | 8.728 |

Bold and italic values in $P < 0.05$. HAD, Hospital Anxiety and Depression; LL, lower limit; OR, odds ratio; UL, upper limit.

or natural disasters.[20] The COVID-19 pandemic can also be accepted as a potentially traumatic event in terms of its characteristics (based on an unknown/unfamiliar danger, unpredictable, prolonged, extreme, and posing a threat of death). The radical changes in people's lifestyles, isolation, fear of infection, and death may have triggered an existential crisis both for themselves and for their loved ones. It is possible that this existential crisis was more severe in immunosuppressed patients and their caregivers. Indeed, PTSD was found in 33.3% of patients and 48.6% of caregivers in our study. Similarly, Cai et al[6] reported the prevalence of pandemic-associated PTSD in solid-organ transplant recipients as 30.5%. Yet, pre-pandemic lifetime prevalence of PTSD is reported as 6.1%-9.2% in the general adult population.[21-23] Compared with these rates, it can be concluded that PTSD significantly increased in liver transplant recipients and caregivers during the pandemic period. Therefore, the prompt identification of at-risk populations such as solid-organ transplant recipients and caregivers, as shown in our study, is important.

Finally, to mention the strengths and limitations of the study, to our knowledge, to date, it is one of the limited number of studies on liver transplant recipients and caregivers during the COVID-19 pandemic period. In addition, caregivers of chronic patients are a special group that has been studied relatively rare, but whose well-being is directly related to the well-being of the care recipient. Including this group in the study can be counted among the strengths of the study. The limitations of the study include the cross-sectional nature of the study, psychopathology assessment was carried out with scales rather than clinical interviews due to the limitations of the pandemic, and the absence of a control group. In addition, the lack of power analysis for the sample size is another limitation. It is not possible for our results to be conclusively attributed to the pandemic. Because our study is a cross-sectional study, it is very difficult to establish a causal relationship. We do not know the pre-pandemic status of high psychopathologies during the pandemic. This is an important limitation of our study.

## Conclusion

Although it may take years and numerous studies to fully understand the sequelae of the COVID-19 pandemic on different subgroups, the present study demonstrates that pandemic and its sequelae have a substantial impact on the mental health of patients with liver transplantation and their primary caregivers and pose a significant risk for the development of mental disorders, including depression, and PTSD. For this vulnerable group, we have a number of recommendations on how to deal with such stressful situations (pandemics or other natural disasters). First of all, regular psychiatric support should be given to organ transplant recipients and caregivers. These people should be referred to psychiatry before and after transplantation. These people should be given psychoeducation on psychiatric diseases. These people should be followed up regularly with psychometric tests. These people should have a fixed psychiatrist and should be followed by the same physician for a long time. Social support programs (nature trips and recreational activities) that can reduce psychopathology in these people should be implemented. Prospective studies should be conducted on organ transplant recipients and their caregivers to evaluate pre-crisis and post-crisis situations in future crises such as pandemics.

**Data Availability Statement:** The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

**Ethics Committee Approval:** Ethical committee approval was received from the Ethics Committee of Akdeniz University (Date: September 9, 2020, Number: KAEK-705).

**Informed Consent:** Written informed consent was obtained from the patients who agreed to take part in the study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – H.A., A.E.; Design – H.A., A.E.; Supervision – H.A., A.E.; Resources – H.A., A.E.; Materials – H.A., A.E.; Data Collection and/or Processing – H.A., A.E.; Analysis and/or Interpretation – H.A., A.E.; Literature Search – H.A., A.E.; Writing Manuscript – H.A., A.E.; Critical Review – H.A., A.E.

**Declaration of Interests:** The authors have no conflict of interest to declare.

**Funding:** The authors declared that this study has received no financial support.

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